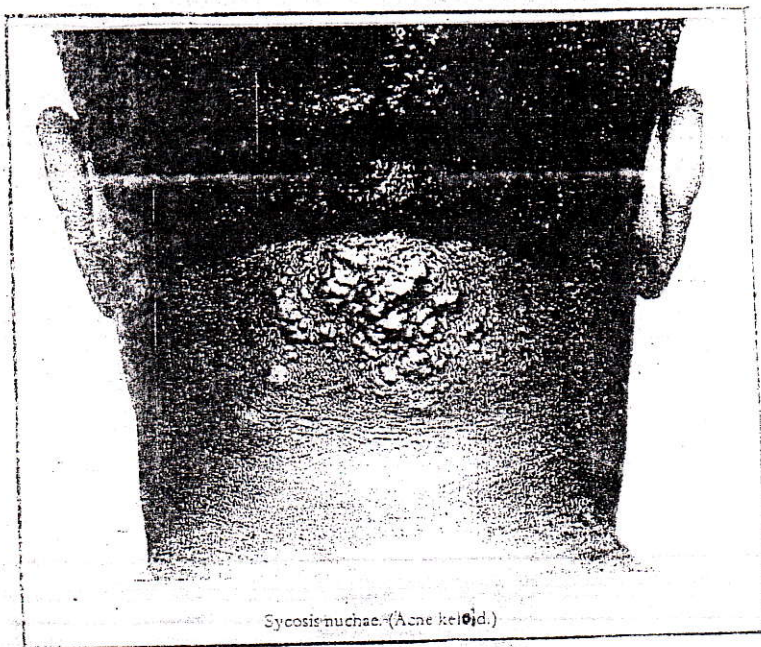


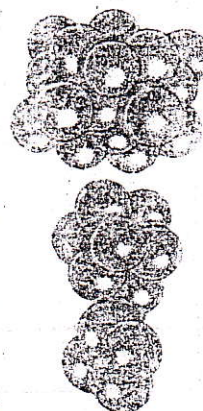
Al Hussein Mohammed Ali Kolaise

GRAM - POSITIVE COCCI

GENUS: STAPHYLOCOCCUS



Sycosis nuchae. (Acne keloid.)



DR. A. PROF. NABEEL AHMED BIN AHMED

Streptococcus
causes
viscous
pus
in
Staph
Aureus.



—Abscess of neck. The arrows indicate fluctuation in two planes.

10.2.15

GRAM – POSITIVE COCCI

There are two medically important genera : Staphylococcus and Streptococcus. The organisms in these genera are nonmotile and do not form spores. Family Micrococcaceae : 1) Genus : Staphylococcus 2) Genus : Micrococcus .

Family Streptococcaceae : 1) Genus : Streptococcus (28 species and subspecies).

STAPHYLOCOCCUS

Diseases Staphylococcus aureus causes abscesses, various pyogenic infections (eg, endocarditis and osteomyelitis), food poisoning, and toxic shock syndrome. It is one of the most common causes of hospital – acquired (NOSOCOMIAL) pneumonia, septicemia, and surgical – wound infections.
* Staphylococcus epidermidis can cause endocarditis and prosthetic joint infections. Staphylococcus saprophyticus causes urinary tract infections.

Important Properties Staphylococci are spherical Gram – positive cocci arranged in irregular grapelike clusters. All staphylococci produce catalase, whereas no streptococci do (catalase degrades H_2O_2 into O_2 and H_2O). Catalase is an important virulence factor because H_2O_2 is microbicidal and its degradation limits the ability of neutrophils to kill.

Three species of staphylococci are human pathogens: S aureus, S epidermidis, and S saprophyticus (Table 7). Of the three, S aureus is by far the most important. S aureus is distinguished from the others primarily by coagulase production (coagulase is an enzyme that causes plasma to clot by activating prothrombin). Furthermore, S aureus usually ferments mannitol and hemolyzes red blood cells, whereas the others do

↓
Carbohydrate

infection with MRSA can range from pneumonia to flesh-eating disease

not. *S. epidermidis* and *S. saprophyticus* are often referred to as coagulase negative staphylococci.

More than 90% of *S. aureus* strains contain plasmids that encode β -lactamase, the enzyme that degrades many, but not all, penicillins. Some strains of *S. aureus* are resistant to the β -lactamase-resistant penicillins, such as methicillin and nafcillin, by virtue of changes in the penicillin-binding protein in their cell membrane. These strains are commonly known as methicillin-resistant *S. aureus*

MRSA

TABLE (7) LABORATORY DIFFERENTIATION OF SPECIES OF THE GENUS STAPHYLOCOCCUS

SPECIES	COAGULASE PRODUCTION	TYPICAL HEMOLYSIS	DNASE TEST	PENICILLIN SENSITIVITY	COLOUR OF THE PIGMENT OF COLONIES
<i>S. aureus</i>	+	Beta Beta Beta	+	R R S	GOLDEN GOLDEN WHITE
<i>S. epidermidis</i>	+	Gamma Beta Gamma	- - + (RARE)	S R S	WHITE WHITE GOLDEN (RARE)
<i>S. saprophyticus</i>	-	Gamma Gamma Beta (Rare)	- - -	S S S	ROUGH-WHITE-GREY ROUGH-WHITE-GREY ROUGH-WHITE-GREY

All staphylococci are catalase – positive.

(MRSA) or nafcillin-resistant *S. aureus* (NRSA). Rare strains called vancomycin – intermediate *S. aureus* (VISA), with reduced sensitivity to vancomycin, have emerged.

S. aureus has several important cell wall components and antigens.

2nd most common cause of UTI in young sexually active females

(1) Protein A is the major protein in the cell wall. It is an important virulence factor because it binds to the Fc protein of IgG at the complement - binding site, (fig 1) thereby , preventing the activation of complement (fig 2). As a consequence, no C3b is produced, and the opsonization and phagocytosis of the organisms are greatly reduced. Protein A is used in certain tests in the clinical laboratory because it binds to IgG and forms a " coagglutinate" with antigen - antibody complexes. The coagulase - negative staphylococci do not produce protein A.

*epidermidis
saprophyticus*

(2) Teichoic acids are polymers of ribitol phosphate. They mediate adherence of the staphylococci to mucosal cells. Antibodies to teichoic acids develop in certain staphylococcal infections, eg, endocarditis.

(3) Surface receptors for specific staphylococcal bacteriophages permit the " phage typing" of strains for epidemiologic purposes. Teichoic acids make up part of these receptors.

(4) Most strains of aureus are coated with a small amount of polysaccharide capsule (microcapsule) that is antiphagocytic. There are (11) serotypes based on antigenicity of the capsular polysaccharide.

(5) The peptidoglycan of S aureus has endotoxin - like properties; ie. it can stimulate macrophages to produce cytokines and can activate the complement and coagulation cascades. This explains the ability of S aureus to cause the clinical findings of septic shock yet not possess endotoxin. (Fig 10) .

Transmission staphylococci are found primarily in the normal human flora. S epidermidis is regularly present on normal skin, and mucous membranes. S aureus is most often found in the nose and sometimes on the skin, especially in hospital staff and patients. Additional sources of

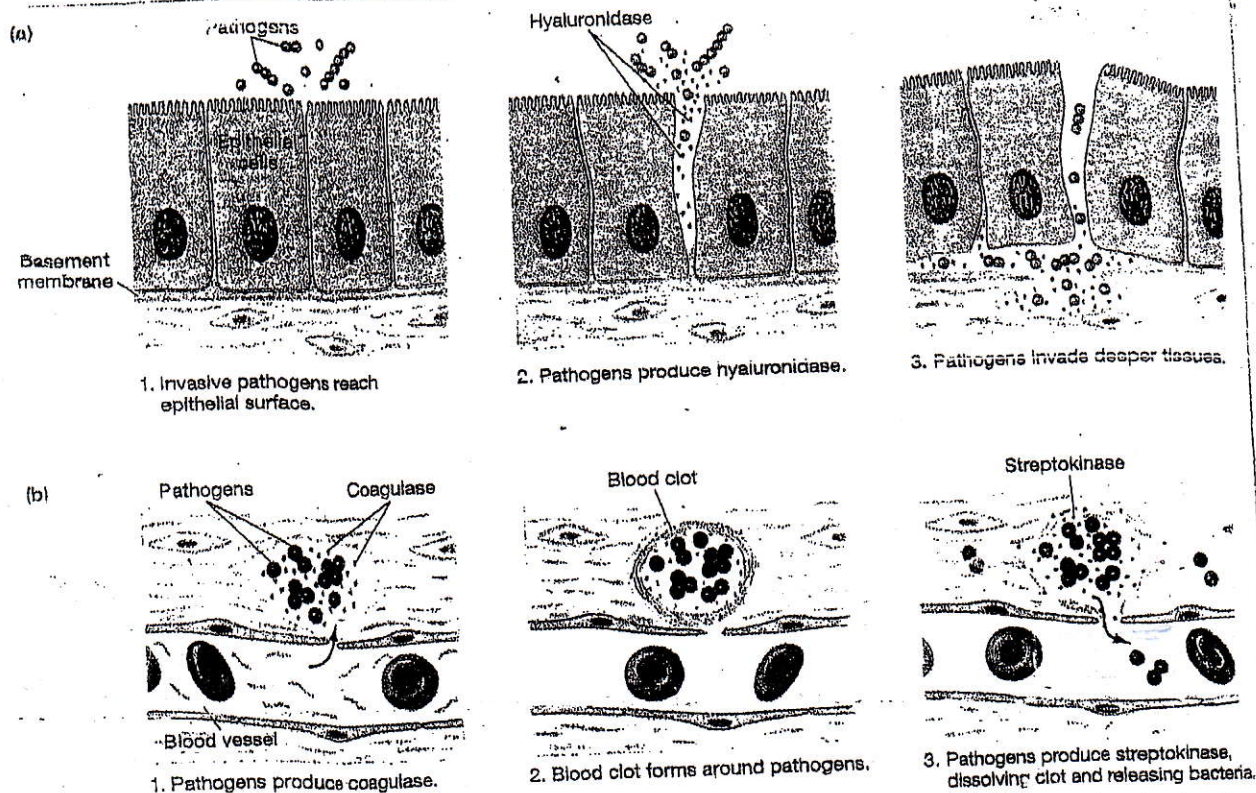
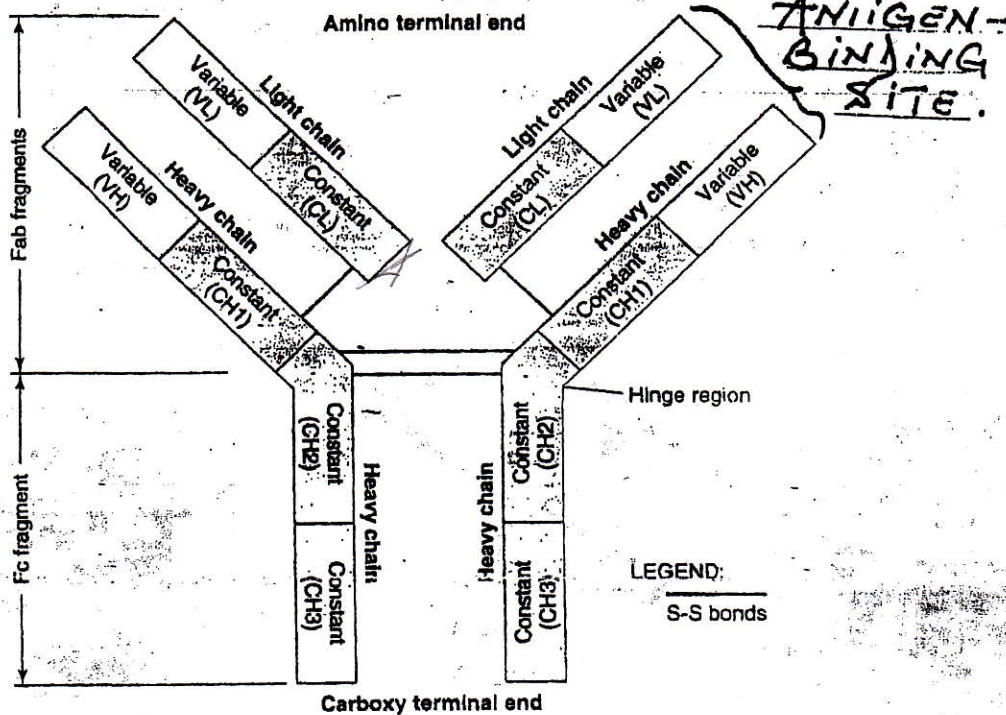


FIGURE 14.5 Enzymatic virulence factors help bacteria invade tissues and evade host defenses. (a) Hyaluronidase dissolves the "cement" that holds together the cells that line the intestinal tract. Bacteria that produce hyaluronidase can then invade deeper cells within the intestinal tissues. (b) Coagulase triggers blood plasma clotting, allowing bacteria protection from immune defenses. Streptokinase dissolves blood clots. Bacteria trapped within a clot can free themselves and spread the infection by producing streptokinase.

TOXINS/ENZYMES:-	ACTIVITY:-
A. TOXINS:-	RBC - LYSIS
1. HEMOLYSINS: $\alpha, \beta, \gamma, \delta$	KILL - LEUCOCYTES EXFOLIATION AND SPLITTING OF EPIDERMIS SHOCK, RASH, DESQUAMATION VOMITING AND DIARRHOEA. <i>Good poisoning</i>
2. LEUCOCIDINS: Alpha-Lysin, Pantov-Valentine-Toxin, Leucolysin	
3. EPIDERMOLYTIC-TOXIN:-	
4. T.S.S-TOXIN:-	
5. ENTEROTOXIN (A-E):-	ACTIVITY:-
B. ENZYMES:-	CLOTS PLASMA.
1. COAGULASE:	↓ BACTERICIDAL-ACTIVITY OF POLYPMN
2. CATALASE:	CONNECTIVE-TISSUE-BREAKDOWN
3. HYALURONIDASE:	DNA-HYDROLYSIS
4. DNASE:	BREAKS LIPIDS OF CELL-MEMB.
5. LIPASE:	-RANGES.
6. PENICILLINASE:	BREAKS DOWN β -LACTAM-DRUGS
7. PROTEIN-A:	ANTI-PHAGOCYTIC.

Fig 1



a/.

Structure of IgG. The Y-shaped IgG molecule consists of two light chains and two heavy chains. Each light chain consists of a variable region and a constant region. Each heavy chain consists of a variable region and a constant region that is divided into three domains: CH1, CH2, and CH3. The CH2 domain contains the complement-binding site, and the CH3 domain is the site of attachment of IgG to receptors on neutrophils and macrophages. The antigen-binding site is formed by the variable regions of both the light and heavy chains. The specificity of the antigen-binding site is a function of the amino acid sequence of the hypervariable regions (see Figure 59-3). (Modified and reproduced, with permission, from Brooks GF et al: *Medical Microbiology*, 20th ed, Originally published by Appleton & Lange. Copyright © 1995 by The McGraw-Hill Companies, Inc.)

~~Fab fragment = ANTIGEN-BINDING FRAGMENT~~

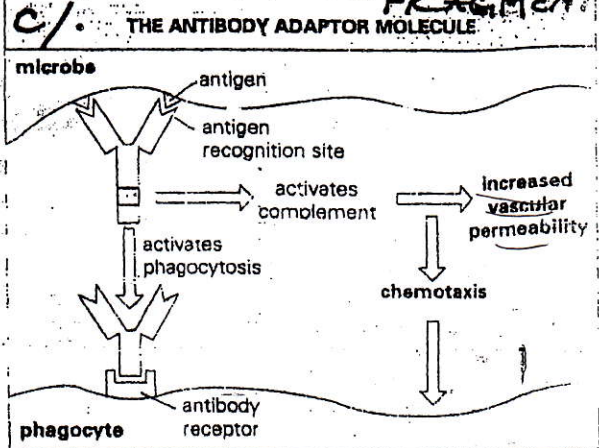


Fig. 5.1 The antigen adaptor molecule. Antibodies (anti-foreign bodies) are produced by host lymphocytes on contact with invading microbes which act as antigen (i.e. generate antibodies). Each antibody has a recognition site enabling it to bind antigen, and a backbone structure capable of some secondary biological action, e.g. activating complement and phagocytosis.

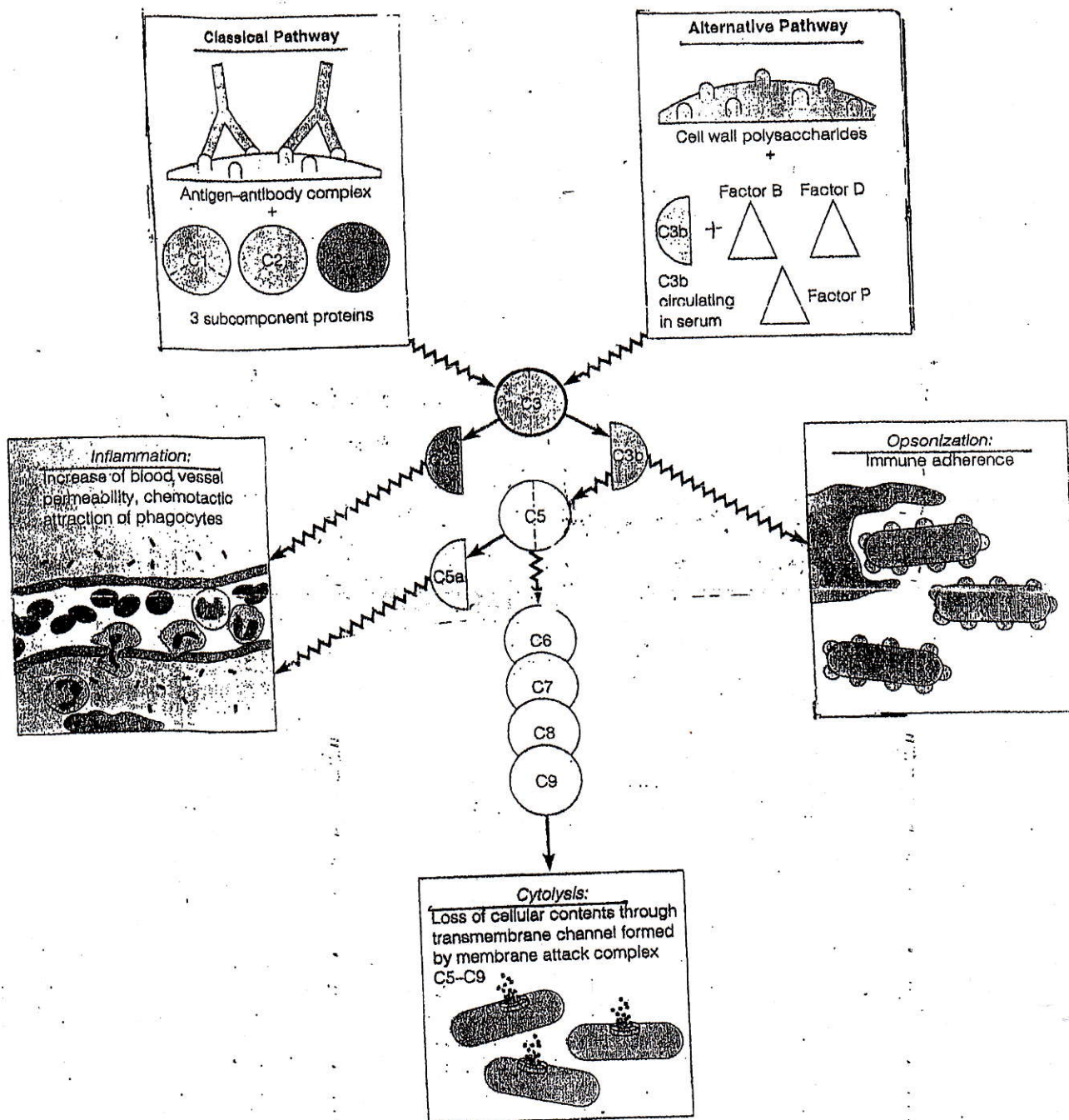


Figure 2 Complement activation via classical and alternative pathways. Events in either the classical or the alternative pathway can initiate the cleavage of C3 into C3a and C3b. These fragments induce three kinds of consequences destructive to microorganisms: cytolysis, inflammation, and opsonization. Complement is a defensive system consisting of at least 20 interacting serum proteins.

INFLAMMATION; THE INFLAMMATORY-RESPONSE CAUSED BY PYOGENIC COCCI, FOR-EXAMPLE, STAPHYLOCOCCUS aureus: -

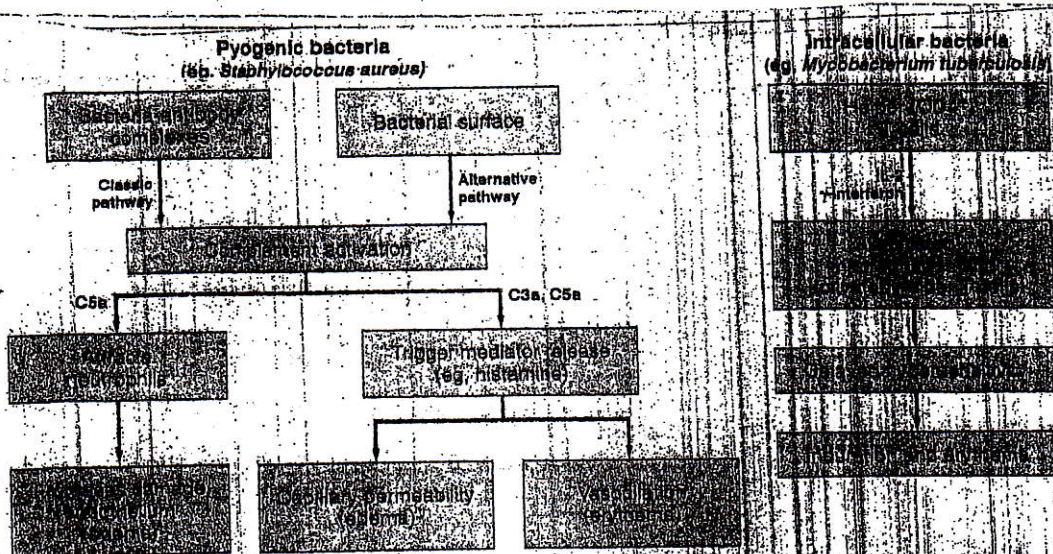


Figure 6-2. Inflammation. The inflammatory response can be caused by two different mechanisms. **Left:** Pyogenic bacteria, eg. *S. aureus*, cause inflammation via antibody- and complement-mediated mechanisms. **Right:** Intracellular bacteria, eg. *M. tuberculosis*, cause inflammation via cell-mediated mechanisms.

staphylococcal infection are shedding from human lesions and fomites contaminated by these lesions. Disease production is favored by a heavily contaminated environment (eg, family members with boils) and a compromised immune system. Low levels of antibody, complement, or neutrophils especially predispose to staphylococcal infections:

Pathogenesis :-

Boils (Furuncles) are the result of infection of the deeper parts of the hair follicles by pyogenic staphylococci. This causes an acute inflammatory reaction ending in suppuration and necrosis.
A carbuncle is a mass of confluent boils.

A. *S aureus* causes disease both by producing toxins and by multiplying in tissue and causing inflammation. The typical lesion of *S aureus* infection is an abscess. Abscesses undergo central necrosis and usually drain to the outside (eg, furuncles - boils), but organisms may disseminate via the bloodstream as well. **Foreign bodies**, such as sutures and intravenous catheters, are important predisposing factors to infection by *S aureus*.

Several important toxins and enzymes are produced by *S aureus*. The three clinically important exotoxins are enterotoxin, toxic shock syndrome toxin, and exfoliation.

(1) **Enterotoxin** causes vomiting and watery, nonbloody diarrhea. It acts as a superantigen⁽¹⁾ within the gastrointestinal tract to stimulate the release of large amounts of interleukin -1 (IL-1) and interleukin -2 (IL-2) from macrophages and helper T cells, respectively. It is fairly heat - resistant and therefore is usually not inactivated by brief cooking. There are six immunologic types of enterotoxin, types A-F, (Fig 10).

(2) **Toxic shock syndrome toxin (TSST)** causes toxic shock, especially in tampon (polyester- foam and polyacrylate rayon) - using menstruating women or in individuals with

1) superantigens - are relatively nonspecific antigens and in -

- discriminatively activate many T - cells receptors at once.

2). ACTIVATED BY PHAGE + TAMPONS SOAK-UP LARGE AMOUNTS OF
MAGNESIUM FROM
VAGINAL - FLUIDS AND
VAGINAL - TISSUES,
THIS ACCELERATES
Staph. aureus to secrete
T.S.S - TOXIN ON THE 4th DAY OF MENSTRUATION.

wound infections. Toxic shock also occurs in patients with nasal packing used to stop bleeding from the nose. TSST is a superantigen and causes toxic shock by stimulating the release of large amounts of IL-1, IL-2, and tumor necrosis factor (TNF) (see the discussions of exotoxins in chapter 7 and superantigens in chapter 58). Approximately 5-25% of isolates of aureus carry the gene for TSST. Toxic shock occurs in people who do not have antibody against TSST (Fig 10).

TSST
① IL1
② IL2
③ TNF

- (3) Exfoliatin causes "scalded - skin" syndrome in young children. It is "epidermolytic" and acts as a protease that cleaves desmosomes, leading to the separation of the epidermis at the granular cell layer.
- (4) Several toxins can kill leukocytes (leukocidins) and cause necrosis of tissues in vivo. Of these, the most important is alpha toxin, which causes marked necrosis of the skin and hemolysis. The cytotoxic effect of alpha toxin is attributed to the formation of holes in the cell membrane and the consequent loss of low - molecular - weight substances from the damaged cell (Fig 11)
- (5) The enzymes include coagulase, fibrinolysin, hyaluronidase, protease, nucleases, and lipases. Coagulase, by clotting plasma, serves to wall of the infection site, thereby retarding the migration of neutrophils into the site. Staphylokinase is a fibrinolysin that can lyse thrombi. Also Dnase, and β Lactamase (penicillinase).

B. S epidermidis and S saprophyticus Unlike S aureus, these two coagulase - negative staphylococci do not produce exotoxins. Thus, they do not cause food poisoning or toxic shock syndrome. They can, however, cause pyogenic infections by eliciting a neutrophilic response. For example, S epidermidis is a prominent cause of

SUPERANTIGENS: -

- 1/ ARE POTENT ANTIGENS.
- 2/ NO NEED FOR INTRACELLULAR-PROCESSION.
- 3/ DIRECT BINDING TO MACROPHAGES.
- 4/ THIS BINDING ACTIVATES HELPER-T-CELLS (TH-CELLS) 100 TIMES THE NORMAL-RATE TO BIND TO MACROPHAGES.
- 5/ MACROPHAGES RELEASE LARGE-AMOUNTS OF IL-1 AND TNF.
- 6/ IL-1 STIMULATES TH-CELLS TO RELEASE LARGE-AMOUNTS OF IL-2 WHICH ENTERS THE BLOOD STREAM WHERE IT CAUSES: -
 - a/ NAUSEA
 - b/ VOMITINGS.
 - c/ FEVER.
- AND d/ SHOCK.
- 7/ MANY TH-CELLS DIE.
- 8/ IMMUNITY IS LOWERED.
- 9/ IMMUNE-TOLERANCE DEVELOPS.
- 10/ AUTOIMMUNE-DISORDER CAN OCCUR, SUCH AS RHEUMATOID-ARTHRITIS AND "MULTIPLE-SCLEROSIS".
- 11/ CAUSE "FOOD-POISONING", "TOXIC-SHOCK-SYNDROME", "SCALDED-SKIN-SYNDROME", AND "FLESH-EATING-NECROTIZING-FASCITIS".

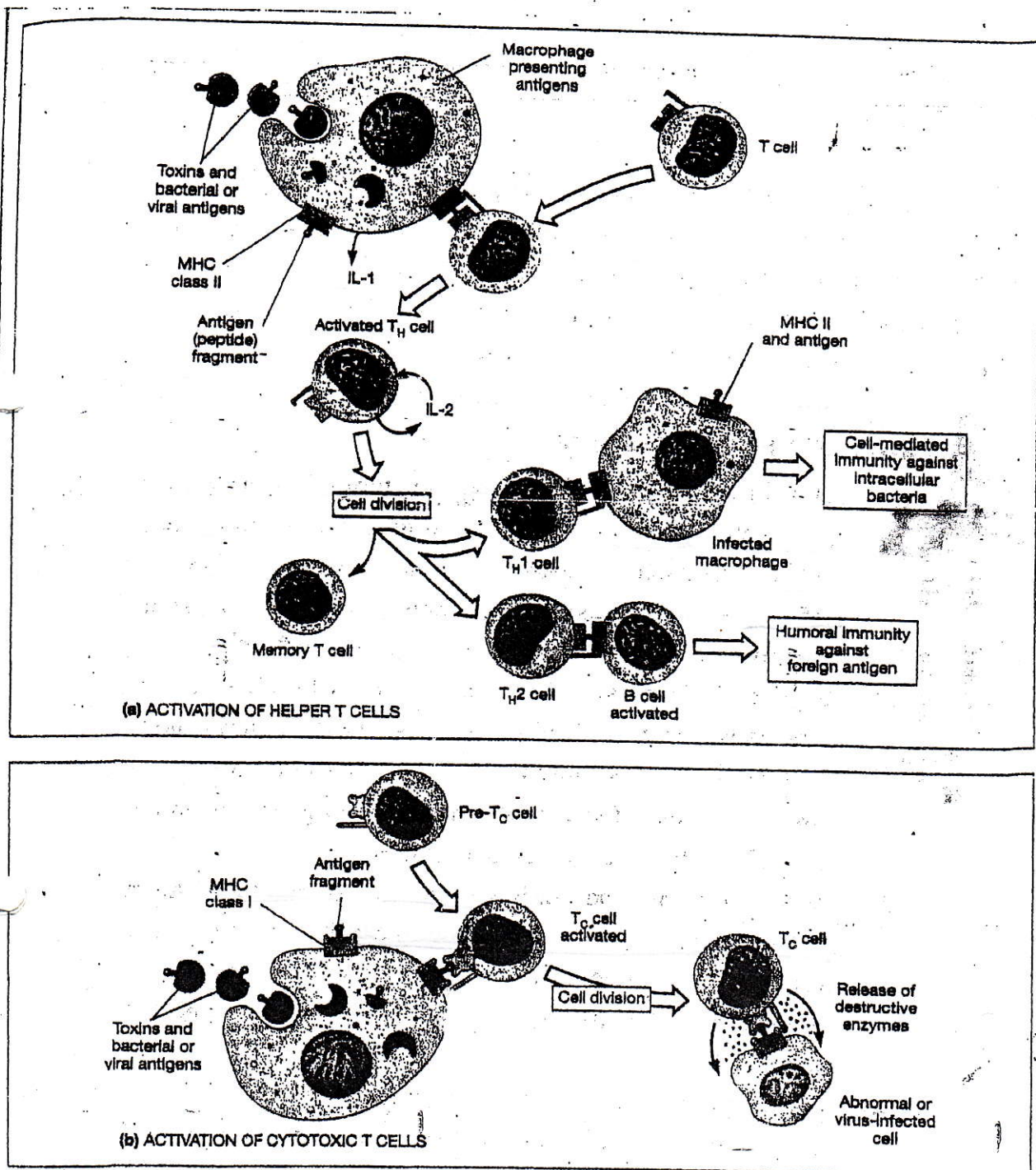


FIGURE 17.13 The reactions in cell-mediated immunity. (a) The macrophage has processed an antigen and inserted an antigen (peptide) fragment into its plasma membrane as an MHC class II molecule. T_H cells have receptors that recognize the peptide fragment on MHC class II. Binding causes the T_H cells to become activated. The activated T cells then differentiate into either T_H1 cells or T_H2 cells. T_H1 cells activate infected macrophages to destroy internal bacterial infections. T_H2 cells activate B cells (humoral immune responses) by binding to MHC class II peptide presented by the B cells. (b) Presenting the same peptide fragment on MHC class I to T_C cells activates cells to attack infected cells, especially abnormal or virus-infected cells.

*S. epidermidis
is a common
cause of prosthetic
infection on prosthetic
infants, surgical
heart valves and
hip joints*

pyogenic infections on prosthetic implants such as heart valves and hip joints.

Clinical findings The important clinical manifestations caused by *S aureus* can be divided into two groups; inflammatory and toxin-mediated. *S aureus* is a major cause of skin, soft tissue, bone, joint, lung, heart, and kidney infections. In the following list, the first six are inflammatory in origin, whereas the last three are toxin-mediated.

A. *S aureus* : Inflammatory .

- (1) Skin infections, including impetigo, furuncles, carbuncles, paronychia, cellulitis, (fig 5) surgical wound infections, eyelid infections (blepharitis), and postpartum breast infections (mastitis), thrombophlebitis of cavernous sinus secondary to a furuncle infection. (figs 3-4 -5-6).
- (2) Septicemia (sepsis) can originate from any localized lesion, especially wound infection, or as a result of intravenous drug abuse. Sepsis caused by *S aureus* has clinical features similar to those of sepsis caused by certain gram - negative bacteria such as *Neisseria meningitidis*.
- (3) Acute bacterial endocarditis on normal or prosthetic heart valves, especially right - sided endocarditis in intravenous drug users (prosthetic valve endocarditis is often caused by *S epidermidis*) frequently fatal within a few days or weeks if untreated.
- (4) Osteomyelitis and arthritis, either hematogenous or traumatic; it is very common cause of osteomyelitis and arthritis, especially in children.

- (5) Pneumonia in postoperative patients or following viral respiratory infection, especially influenza (staphylococcal pneumonia often leads to empyema).
- (6) Abscesses (metastatic) in any organ, after bacteremia.

B. S aureus : Toxin – Mediated

- (1) Food poisoning (characterized by vomiting being more prominent than diarrhea) caused by ingestion of enterotoxin, which is preformed in foods and hence has a short incubation period (1-8 hours);
- (2) Toxic shock syndrome, which includes fever, hypotension, and a diffuse, macular, sunburn-like rash that goes on to desquamate, and involvement of three or more of the following organs: liver, kidney, GI tract, central nervous system, muscle, or blood; (fig 7).
- (3) Scalded skin syndrome, in which the superficial layers of the epidermis slough in response to the presence of exfoliatin. (figs 8-9).

exfoliation
epidermolytic toxin

C. S epidermidis and S saprophyticus .

There are two coagulase – negative staphylococci of medical importance: S epidermidis and S saprophyticus. S epidermidis infections are almost, always hospital – acquired, whereas S saprophyticus infections are almost always community – acquired.

S epidermidis is part of the normal human flora on the skin and mucous membranes but can cause infections of intravenous catheters and prosthetic implants, eg, heart valves, vascular grafts, and joints. S epidermidis is also a major cause of sepsis in neonates and of peritonitis in patients with renal failure who are undergoing peritoneal dialysis through an indwelling catheter. It is the most common bacterium to cause cerebrospinal

glycocalyx
epidermidis

fluid shunt infections. Strains of epidermidis that produce a glycocalyx are more likely to adhere to prosthetic implant materials and therefore are more likely to infect these implants than strains that do not produce a glycocalyx. Hospital personnel are a major reservoir for antibiotic - resistant strain of S epidermidis.

S saprophyticus causes urinary tract infections, particularly in sexually active young women. Most women with this infection have had sexual intercourse within the previous 24 hours. This organism is second to E coli as a cause of community - acquired urinary tract infections in young women.

Laboratory diagnosis smears from staphylococcal lesions reveal Gram - positive cocci in grapelike clusters. Cultures of S aureus typically yield golden - yellow colonies that are usually beta hemolytic. S aureus is coagulase - positive. Mannitol - salt agar is a commonly used screening device for S aureus. Cultures of coagulase - negative staphylococci typically yield white colonies that are nonhemolytic. The two coagulase - negative staphylococci are distinguished by their reaction to the antibiotic novobiocin: S epidermidis is sensitive, whereas S saprophyticus is resistant. There are no generally useful serologic or skin tests. In toxic shock syndrome, isolation of S aureus is not required to make a diagnosis as long as the clinical criteria are met. Phage typing for epidemiological surveys (table 15-2).

Treatment in the united states, 90% or more of S aureus strains are resistant to penicillin G. Most strains produce β - lactamase under control of transmissible plasmids. Such organisms can be treated with β - lactamase - resistant penicillins, ege, nafcillin or cloxacillin, some cephalosporins, or vancomycin. Treatment with a combination of a β - lactamase- sensitive penicillin, ege, amoxicillin, and a β - lactamase inhibitor, ege, clavulanic acid, is also useful. Approximately 20% of S aureus strains

Jan

Novobiocin

sensitive epidermidis

Resistant saprophyticus

naftillin
CLOxacillin

PBP
+ transpeptidase

are : methicillin-resistant (or " naftillin-resistant ") by virtue of altered penicillin-binding proteins. Such organisms can produce sizable outbreaks of disease, especially in hospitals. The drug of choice for these staphylococci is vancomycin, to which gentamicin is sometimes added. Strains of *S aureus* with intermediate resistance (so - called **VISA strains**) and with complete resistance to vancomycin have been isolated from patients. These strains are typically methicillin / naftillin-resistant as well, which makes them very difficult to treat. A combination of two streptogramins, quinupristin - dalfopristin (synercid), has been shown to be effective , but synercid is available only as investigational drug at this time. Streptogramins inhibit bacterial protein synthesis in a manner similar to macrolides but are bactericidal for *S aureus*.

4-8 Mg/mL
MIC

VRSA
and VISA
strains
treated
with a
combination
of
(Streptogramin
Quinupristin
dalfopristin
Synercid

W

The treatment of toxic shock syndrome involves correction of the shock using fluids, pressor drugs, and inotropic drugs ; administration of a β - lactamase resistant penicillin such as naftillin ; and removal of the tampon or debridement of the infected site as needed. Pooled serum globulins, which contain antibodies against TSST, may be useful.

Mupirocin is very effective as a topical antibiotic in skin infections caused by *S aureus*. It also has been used to reduce nasal carriage of the organism in hospital personnel and in patients with recurrent staphylococcal infections.

Some strains of staphylococci exhibit **tolerance**; ie, they can be inhibited by antibiotics but are not killed (the ratio of MBC to MIC is very high). Tolerance may result from failure of the drugs to inactivate inhibitors of autolytic enzymes that degrade the organism. Tolerant organisms should be treated with drug combinations.

Drainage (spontaneous or surgical) is the cornerstone of abscess treatment. Previous infection provides only partial immunity to reinfection. *S epidermidis* is highly antibiotic resistant. Most strains produce β -lactamase and many are methicillin / naftillin-resistant. The drug of choice is vancomycin to which either rifampin or an aminoglycoside can be added. Removal of the catheter or other device is often necessary. *S saprophyticus*

Write in Details about
Penicillin

Phagetyping of Staph aureus Strains.

Table 15-2

31

24 Piece

29		52	
52A	79	80	
3A	3C		55
71	6	42A	53
54	75	77	83A
84	85		81
94	95		96



urinary tract infections can be treated with a quinolone, such as norfloxacin, or with trimethoprim-sulfamethoxazole.

co-trimoxazole

Prevention There is no effective immunization with toxoids or bacterial vaccines. Cleanliness, frequent hand - washing, and aseptic management of lesions help to control spread of *S aureus*. Persistent colonization of the nose by *S aureus* can be reduced by intranasal mupirocin or by oral antibiotics, such as ciprofloxacin or trimethoprim-sulfamethoxazole, but is difficult to eliminate completely. Shedders may have to be removed from high - risk areas, eg, operating rooms and newborn nurseries. Cefazolin is often used perioperatively to prevent staphylococcal surgical wound infections.

For weaker persons

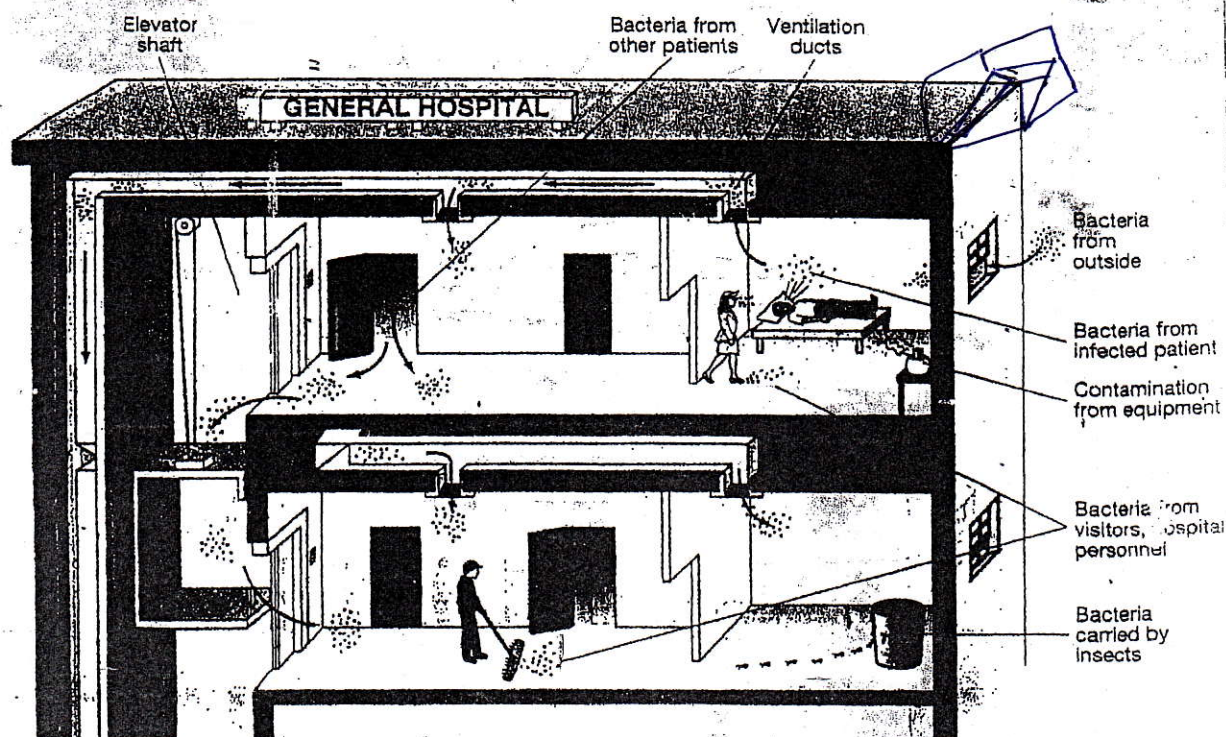


FIGURE 15.20 Some common modes of transmission of nosocomial infections in a hospital.

Fig 3 . SPECIAL INFECTIONS OF THE FACE

Boils and 'Pimples' in the region of the 'danger' (mask) area of the face (fig. 532) should never be squeezed, pricked, or incised, for by so doing the infection can reach the cavernous sinus by the venous connections (fig. 533) and cause cavernous sinus thrombosis (fig. 534), a fatal condition in the pre-antibiotic days.

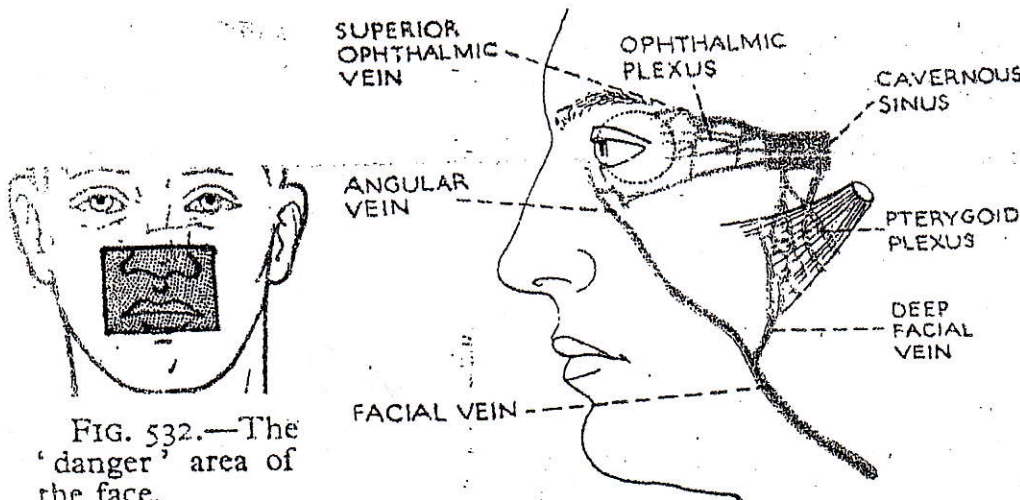


FIG. 532.—The 'danger' area of the face.

FIG. 3.—The cavernous sinus and its connections.
(VENOUS SPACE IN DURA MATTER)



FIG. 534.—Thrombophlebitis of the cavernous sinus secondary to a furuncle of the nose. (P. Read, F.R.C.S., London.)



Fig. 4. Impetigo is a condition limited to the epidermis, with typically yellow, crusted lesions. It is commonly caused by *Strep. pyogenes* either alone or together with *Staph. aureus*. Courtesy of M.J. Wood.

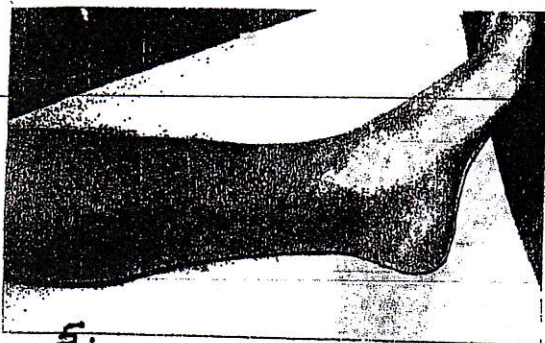


Fig. 5. Folliculitis. A superficial infection shown here localized in the hair follicles on the forearm. The boils contain creamy-yellow pus and masses of bacteria. *Staphylococcus aureus* is the most common cause. Courtesy of A du Vivier.

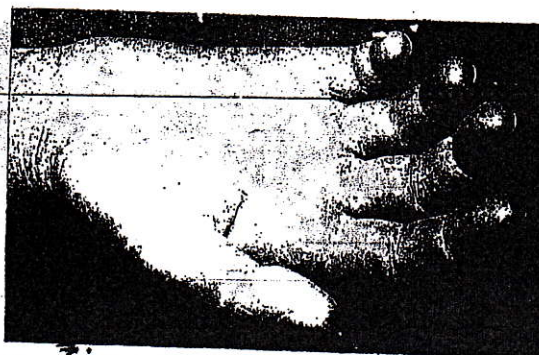


Fig. 7. Toxic shock syndrome results from systemic infection with *Staph. aureus* but has skin manifestations in the form of desquamation particularly of the palm and soles. Courtesy of MJ Wood.

Fig 7.



Fig. 8. Scalded skin syndrome results from infection of the skin with strains of *Staph. aureus* producing a specific toxin which destroys the intercellular connections in the skin resulting in large areas of desquamation. The appearance may be confused with a burn. Courtesy of A du Vivier.



Fig. 9. Staphylococcal scalded skin syndrome. There are large areas of epidermal loss where bullae have burst. Courtesy of L. Brown.



Fig. 12. Erysipelas. Infection with *Streptococcus pyogenes* involving the dermal lymphatics and giving rise to a clearly demarcated area of erythema and induration. When the face is involved there is often a typical 'butterfly-wing' rash, as shown here. Courtesy of MJ Wood.



Fig. 6. Gram-positive cocci in pus.



Fig. 9. When the focus of infection is in the subdermal fat cellulitis, a severe and rapidly progressive infection is the typical presentation. Large blisters and scabs may also be present on the skin surface. Courtesy of MJ Wood.



FIG. 2.
Impetigo contagiosa.

HIDRADENITIS :- STAPH. AUREUS INFECTION OF AXILLARY
APOCRINE - SWEAT
GLANDS.

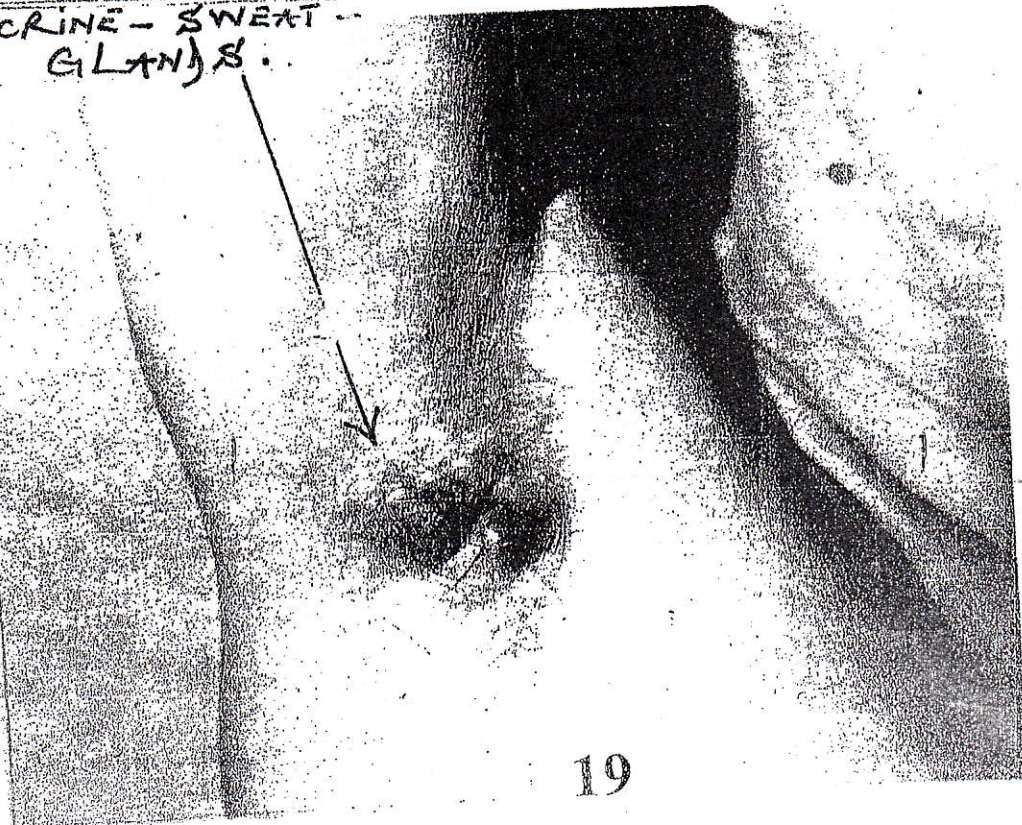


fig 17 • Cellulitis

A suppurative inflammation of the subcutaneous and fascial planes.



- Cellulitis usually presents with a well demarcated area of inflammation
- Redness, heat, swelling and pain are the cardinal signs of inflammation
- Fatal gangrene can occur .

fig 18 • Orbital cellulites



Cavernous Sinus Thrombosis (C.S.T)

THIS IS THE FORMATION OF AN INFECTED - BLOOD - CLOT (THROMBUS) IN ONE OF THE CAVERNOUS - SINUSES.

The two cavernous sinuses are large veins lying within the skull cavity, immediately behind each eye socket (orbit) and on either side of the pituitary gland. They connect with the veins of the face and those of the brain.

The cavernous sinuses receive venous blood from the facial veins (via the superior and inferior ophthalmic veins) as well as the sphenoid and middle cerebral veins. They, in turn, empty into the inferior petrosal sinuses, then into the internal jugular veins and the sigmoid sinuses via the superior petrosal sinuses.

This complex web of veins contains no valves; blood can flow in any direction depending on the prevailing pressure gradients.

The internal carotid artery with its surrounding sympathetic plexus passes through the cavernous sinus. The third, fourth, and sixth cranial nerves are attached to the lateral wall of the sinus. The ophthalmic and maxillary divisions of the fifth cranial nerve are embedded in the wall.

This intimate juxtaposition of veins, arteries, nerves, meninges, and paranasal sinuses accounts for the characteristic etiology and presentation of CST: (Figs. 1 and 2).

The network of veins that runs back to join the cavernous sinuses carries blood mainly from a triangular area centred around the nose. Any infection in this area, as from a pimple or boil in the nostril or on the upper lip or nose, may cause a local tissue inflammation known as cellulitis. From this local inflammation, infection may spread backwards by way of the veins to reach, and involve, one of the cavernous sinuses. If this happens, the blood in the sinus may turn to an infected clot, with potentially very serious consequences. This is a cavernous sinus thrombosis. (FURUNCLE)

Mortality/Morbidity: Prior to the advent of effective antimicrobial agents, the mortality rate from CST was effectively 100%. Typically, death is due to sepsis or central nervous system (CNS) infection. With aggressive management, the mortality rate is now less than 30%. Morbidity, however, remains high, and complete recovery is rare. Roughly one sixth of patients are left with some degree of visual impairment, and one half have cranial nerve deficits.

Causes:

- Most cases of septic CST are due to an acute infection in an otherwise healthy individual. However, patients with chronic sinusitis or diabetes mellitus may be at a slightly higher risk.
- The causative agent is generally *Staphylococcus aureus*, although streptococci, pneumococci, and fungi may be implicated in rare cases.

Race: No predilection

Sex: No predilection

Age: All ages are affected, with a mean of 22 years.

1. Internal carotid artery
2. Vertebral artery
3. Cavernous sinus
4. Carotid canal
5. Anterior cerebral artery
6. Posterior cerebral artery

Fig 19.

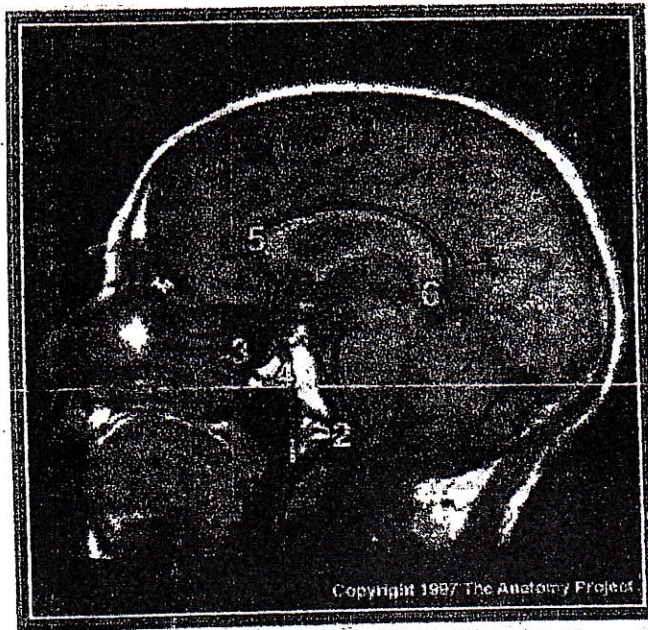
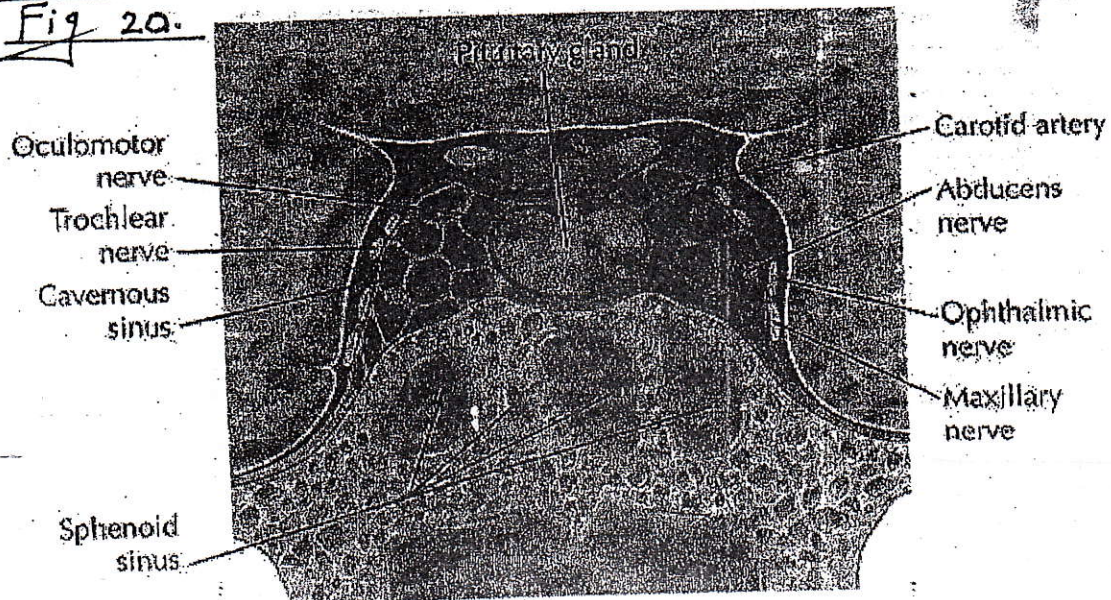


Fig 20.



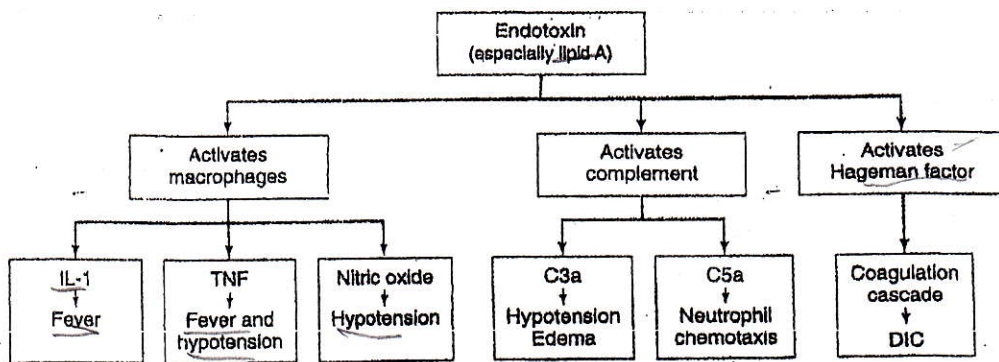


Figure 7-4. Mode of action of endotoxin. Endotoxin is the most important cause of septic shock, which is characterized primarily by fever, hypotension, and disseminated intravascular coagulation (DIC). Endotoxin causes these effects by activating three critical processes: (1) activating macrophages to produce interleukin-1 (IL-1), tumor necrosis factor (TNF), and nitric oxide; (2) activating complement to produce C3a and C5a; and (3) activating Hageman factor, an early component of the coagulation cascade.

Table 7-10. Effects of endotoxin.

Clinical Findings ¹	Mediator or Mechanism
Fever	Interleukin-1
Hypotension (shock)	Bradykinin, nitric oxide
Inflammation	Alternative pathway of complement (C3a, C5a)
Coagulation (DIC) ²	Activation of Hageman factor

¹Tumor necrosis factor triggers many of these reactions.
²DIC, disseminated intravascular coagulation.

Endotoxins: Endotoxins are integral parts of the cell walls of both gram-negative rods and cocci, in contrast to exotoxins, which are released from the cell (Table 7-6). In addition, several other features distinguish these substances. Endotoxins are lipopolysaccharides (LPS), whereas exotoxins are polypeptides; the enzymes that produce the lipopolysaccharide are encoded by genes on the bacterial chromosome, rather than by plasmid or bacteriophage DNA, which usually encodes the exotoxins. The toxicity of endotoxins is low in comparison with that of exotoxins. All endotoxins produce the same generalized effects of fever and shock, although the endotoxins of some organisms are more effective than those of others (Figure 7-4). Endotoxins are weakly antigenic; they induce protective antibodies so poorly that multiple episodes of toxicity can occur. No toxoids have been produced from endotoxins, and endotoxins are not used as antigens in any available vaccine.

The findings of fever and hypotension are salient features of septic shock. The endotoxins of gram-negative bacteria are the best-established causes of septic shock, but surface molecules of gram-positive bacteria (which do not have endotoxins) can also cause septic shock (see below). Two features of septic shock are interesting:

(1) Septic shock is different from toxic shock. In septic shock, the bacteria are in the bloodstream, whereas in toxic shock, it is the toxin that is circulating in the blood. The clinical importance of this observation is that in septic shock, blood cultures are usually positive, whereas in toxic shock, they are usually negative.

(2) Septic shock can cause the death of a patient even though antibiotics have killed the bacteria in the patient's blood; ie, the blood cultures have become negative. This occurs because septic shock is mediated by cytokines, such as tumor necrosis factor and interleukin-1 (see below), that continue to act even though the bacteria that induced the cytokines are no longer present.

Endotoxins

- integral parts of the cell wall of both gram-negative rods and cocci

- lipopolysaccharides

- encoded by genes on the bacterial chromosome

- low toxicity

- weak antigenic

exotoxins

- released from the cell of gram +

- polypeptides

- encoded by plasmids or bacteriophage DNA

- High toxicity

- High antigenic

The structure of the LPS is shown in Figure 2-6. The toxic portion of the molecule is **lipid A**, which is composed of disaccharides with several fatty acids attached. β -Hydroxymyristic acid is always one of the fatty acids and is found only in lipid A. The other fatty acids differ according to species. The polysaccharide core in the middle of the molecule protrudes from the surface of the bacteria and has the same chemical composition within members of a genus. The repeat unit of sugars on the exterior differs in each species and frequently differs between strains of a single species. It is an important antigen of some gram-negative rods ("O" or somatic antigen) and is composed of three, four, or five sugars repeated up to 25 times. Because the number of permutations of this array is very large, many antigenic types exist. For example, more than 1500 antigenic types have been identified for *Salmonella*.

The biologic effects of endotoxin (Table 7-10) include

- (1) Fever due to the release by macrophages of endogenous pyrogen (interleukin-1), which acts on the hypothalamic temperature-regulatory center
- (2) Hypotension, shock, and impaired perfusion of essential organs owing to bradykinin-induced vasodilation, increased vascular permeability, and decreased peripheral resistance (nitric oxide, a potent vasodilator, also causes hypotension)
- (3) Disseminated intravascular coagulation (DIC) due to activation of the coagulation system through Hageman factor (factor XII), resulting in thrombosis, a petechial or purpuric rash, and tissue ischemia
- (4) Activation of the alternative pathway of the complement cascade, resulting in inflammation and tissue damage
- (5) Activation of macrophages, increasing their phagocytic ability, and activation of many clones of B lymphocytes, increasing antibody production. (Endotoxin is a polyclonal activator of B cells, but not T cells.)

The evidence that endotoxin causes these effects comes from the following two findings: (1) purified lipopolysaccharide, free of the organism, reproduces the effects; and (2) antiserum against endotoxin can mitigate or block these effects.

Clinically, the presence of DIC in the patient can be assessed by the D-dimer laboratory test. D-dimers are cleavage products of fibrin (fibrin split products) that are detected in the blood of patients with DIC.

Endotoxins do not cause these effects directly. Rather, they elicit the production of host factors such as **interleukin-1** and **cachectin**¹ (tumor necrosis factor, TNF) from macrophages.² TNF is the central mediator because purified recombinant TNF reproduces the effects of endotoxin and antibody against TNF blocks the effects of the endotoxin. Endotoxin also induces macrophage migration inhibitory factor, which recent studies have shown plays a powerful role in the induction of septic shock.

Note that TNF in small amounts has beneficial effects, eg, causing an inflammatory response to the presence of a microbe, but in large amounts, it has detrimental effects, eg, causing septic shock and DIC. It is interesting that the activation of platelets, which results in clot formation and the walling-off of infections, is the same process that, when magnified, causes DIC and the necrosis of tumors. It is the ability of TNF to activate platelets that causes intravascular clotting and the consequent infarction and death of the tumor tissue. The symptoms of certain autoimmune diseases such as rheumatoid arthritis are also mediated by TNF; however these symptoms are not induced by endotoxin but by other mechanisms, which are described in Chapter 66. Some of the important beneficial and harmful effects of TNF are listed in Table 7-11.

Endotoxins can cause a pyrogenic response in the patient if they are present in intravenous fluids. In the past, intravenous fluids were sterilized by autoclaving, which killed any organisms present but resulted in the release of endotoxins that were not heat-inactivated. For this reason, these fluids are now sterilized by filtration, which physically removes the organism without releasing its endotoxin. The contamination of intravenous fluids by endotoxin is detected by a test based on the observation that nanogram amounts of endotoxin can clot extracts of the horseshoe crab, *Limulus*.

Endotoxinlike pathophysiologic effects can occur in gram-positive bacteremic infections (eg, *S aureus* and *S pyogenes* infections) as well. Since endotoxin is absent in these organisms, other cell wall components, eg, teichoic acid or peptidoglycan, probably cause the release of TNF and interleukin-1 from macrophages.

1 X 9
X 10
X 11
X 11 1/2

